

## Elusive Pancreatic Stem Cells Found In Mice

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Just as many scientists had given up the search, researchers have discovered that the pancreas does indeed harbor stem cells with the capacity to generate new insulin-producing beta cells. If the finding made in adult mice holds for humans, the newfound progenitor cells will represent "an obvious target for therapeutic regeneration of beta cells in diabetes," the researchers report in the Jan. 25 issue of *Cell*.

"One of the most interesting characteristics of these [adult] progenitor cells is that they are almost indistinguishable from embryonic progenitors," said Harry Heimberg of the JDRF Center at Vrije Universiteit Brussel in Belgium and the Beta Cell Biology Consortium. "In terms of their structure and gene expression, there are no major differences. They look and behave just like embryonic beta cell progenitors."

Insulin is required for cells to take up blood sugar, the body's primary energy source. In people with certain types of diabetes, blood sugar rises due to an inability of pancreatic beta cells to produce insulin in sufficient quantities.

Previous studies had failed to demonstrate the existence of bona fide beta cell progenitors in the pancreas after birth. The elusiveness of this cell type reached a summit when genetic lineage tracing provided evidence that pre-existing beta cells, rather than stem/progenitor cells, are the major source of new beta cells in adult mice, the researchers said. "Most people gave up looking because they are so few and so hard to activate," Heimberg said.

In the new study, Heimberg's team tied off a duct that drains digestive enzymes from the pancreas. That injury led to a doubling of beta cells in the pancreas within two weeks, they showed. The animals' pancreases also began producing more insulin, evidence that the new beta cells were fully functional, Heimberg said. He suspects the regenerative process is sparked by an inflammatory response in the enzyme-flooded pancreas.

They further found that the production of new beta cells depends on a gene called Neurogenin 3 (Ngn3), which is known to play a role in the pancreas during embryonic development.

"The most important challenge now is to extrapolate our findings to patients with diabetes," Heimberg said. Although he cautioned that any potential diabetes treatment remains far into the future, "our findings reveal the significance of investigating the feasibility of (1) isolating facultative beta cell progenitors and newly formed beta cells from human pancreas in order to expand and differentiate them in vitro and transplant them in diabetic patients and (2) composing a mix of factors able to activate beta cell progenitors to expand and differentiate in situ in patients with an absolute or relative deficiency in insulin," the researchers wrote.

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